REMARKS

Claims 51-102 are pending. Claims 51-58, 67 and 96-102 are under examination.

Applicants note that the only rejection of claims 58 and 67 is an obviousness-type double patenting rejection. Applicants respectfully submit that the additional species claims that depend from generic linking claim 58 and which are currently withdrawn, claims 59-66 and 68-73, should be rejoined.

Rejections Under 35 U.S.C. § 112

The rejection of claims 51-57 and 96-102 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicants respectfully maintain that the specification provides sufficient description and guidance for the claimed compositions.

The Court of Appeals for the Federal Circuit ("Federal Circuit") has provided substantial guidance regarding the written description requirement of 35 U.S.C. § 112 and satisfaction of the "possession test." The Federal Circuit has instructed that compliance with the written description requirement is to be assessed from the viewpoint of one of ordinary skill in the art. See *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1117 (Fed.Cir.1991) ("the applicant must ... convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention"). The Federal Circuit also has instructed that compliance with the written description requirement does not require a patent specification to describe exactly the claimed subject matter; rather the specification must show the skilled artisan that the applicant invented what is claimed. See *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) ("The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed'"(citations omitted)). The Federal Circuit also has instructed that "[t]he disclosure rule does not require a particular form of disclosure." *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1321, 66 USPQ2d 1429, 1439 (Fed. Cir. 2003).

The Office Action refers to the written description guidelines and the indication that a satisfactory disclosure requires a "representative number" of species. The Office Action further indicates that satisfactory disclosure depends on whether one skilled in the art would recognize that Applicant was in possession of the "necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." Applicants respectfully maintain, for the reasons of record, that the specification teaches a sufficient number of species representative of the claimed genus. As discussed in the previously filed response, the specification teaches a variety of polymerase mutants having one or more amino acid substitutions in the O-helix of a parent thermostable polymerase (see Examples V and VI, pages 51-55). Accordingly, Applicants maintain that the disclosed species provide sufficient teaching of the common attributes and features of the claimed genus.

In the Office Action, it is asserted that "Applicant has one common attribute," the presence of a mutation in the O-helix. However, it is respectfully pointed out that the claimed compositions have multiple common structural and functional attributes. In addition to the presence of an amino acid mutation in the O-helix, the genus of claim 51 is directed to a thermostable polymerase mutant having polymerase activity and higher fidelity than the parent thermostable polymerase. Applicants contend that the exemplary species have multiple structural and functional attributes and are representative of the claimed genus.

In the Office Action, it is asserted that the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification since they are not limited to any particular SEQ ID NO. Applicants point out that the claims are directed to compositions containing polymerase mutants and not nucleic acids. Furthermore, Applicants respectfully draw the Examiner's attention to claim 96, which recites a specific SEQ ID NO for the polymerase. Thus, in contrast to the assertion in the Office Action, claim 96 and its dependent claims recite a specific SEQ ID NO. Moreover, Applicants respectfully disagree with the assertion that the claims encompass a genus of nucleic acids which are different from those disclosed in the specification. Applicants maintain that the species disclosed in the specification are representative of the claimed genus and that the genus does encompass the disclosed species.

The Office Action further indicates that the claimed genus includes variants for which no written description is provided in the specification and that there are a large number of possible mutations in the O-helix. As discussed in the previous response, the claimed compositions contain polymerase mutants having polymerase activity and higher fidelity than the parent thermostable polymerase and, therefore, the claimed genus encompasses only those mutants having the recited characteristics. Thus, the genus is not the number of all possible O-helix mutants but those O-helix mutants having polymerase activity and higher fidelity than the parent thermostable polymerase. Furthermore, the written description requirement for a claimed genus can be satisfied through sufficient description of a representative number of species. Moreover, the MPEP indicates that "[D]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces" (MPEP § 2163 II (3)(a)(ii)).

An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Applicants respectfully submit that, based on the teachings in the specification and what was well known in the art, one skilled in the art would have readily recognized that Applicants invented the claimed compositions.

Applicants respectfully disagree with the assertion in the Office Action that there is no showing or evidence that links structural limitations regarding single or multiple mutations of the O-helix to the particular functional limitations of higher fidelity and that there is no theory or method taught by Applicant that permits selection of higher fidelity mutants. To the contrary and as discussed in the previous response, the specification teaches how to generate a large number of polymerase mutants and screen for polymerase mutants having polymerase activity and higher fidelity than the parent thermostable polymerase (page 14, line 4, to page 16, line 14; Example I, pages 33-41, and Example V, pages 51-53). Therefore, Applicants respectfully submit that it would be routine for one skilled in the art to screen and identify polymerase mutants having the recited characteristics.

The Office Action also refers to *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Applicants respectfully direct the Examiner's attention to the more recent Federal Circuit decisions that have explicitly distinguished the *Lilly* decision.

In the recent decision of *Moba v. Diamond Automation*, 325 F.3d 1306, 66 USPQ2d 1429 (Fed.Cir. 2003) the Federal Circuit stated:

> [C]ase law reflects two applications of [the written description requirement,] . . . "[t]he function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him. . . .In that setting, the written description is the metric against which a subsequently added claim is measured to determine if it is due the priority date of the original patent. . . . The second application of the written description requirement is reflected in *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997). There, this court invoked the written description requirement in a case without priority issues, [requiring a] precise definition of a DNA sequence in the patent specification. **In more recent cases, however, this court has distinguished *Lilly*. . . . The *Lilly* disclosure rule does not require a particular form of disclosure** because one of skill could determine from the specification that the inventor possessed the invention at the time of filing.

Id. at 1319 (Emphasis added).

Similarly, in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002), after initially holding that a reference to specified biological material in a public depository was not a sufficient written description, the court on rehearing indicated that *Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement and held the written description requirement may be satisfied if, in the knowledge of the art, the disclosed function is sufficiently correlated to a particular, known structure.

In its first pronouncement following *Enzo*, the Federal Circuit again noted:

> More recently, in *Enzo Biochem*, we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, **the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.**

Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1399 (Fed. Cir. 2003)(Emphasis added).

Furthermore, the Federal Circuit recently extended this rationale to binding polypeptides such as antibodies in *Noelle v. Lederman*, 355 F.3d 1343, 69 USPQ 1508 (Fed. Cir. 2004). The Court in *Noelle* stated that written description for antibodies relying on functional characteristics can be met if function is coupled with a disclosed correlation to a known structure.

Applicants respectfully maintain that the specification provides teachings that sufficiently correlate function with structure. Measured according to the Federal Circuit's extensive instructions, Applicant's specification fully supports the currently pending claims. Applicant's specification allows those of skill in the art to recognize that Applicants invented what is claimed.

In the Office Action, it is asserted that the definition of proteins as having a mutation in the O-helix and higher fidelity lacks any specific structure which is correlative with function. As discussed above, the Court has held that written description can be satisfied if the function is sufficiently correlated to a specific, known structure. Applicants respectfully submit that the specification teaches a sufficient correlation of the functional activity of higher fidelity polymerase activity with a known structure. In particular, the specification teaches exemplary species having a mutation in the O-helix and the structures of these higher fidelity mutants (see Example V, pages 51-53 and Tables II and IV). Accordingly, Applicants respectfully submit that the specification teaches a sufficient correlation of the function of the claimed polymerase mutants and known structure and therefore provides sufficient description and guidance to satisfy the written description requirement.

In light of the teachings in the specification and what was well known in the art, as discussed above, Applicants contend that there is sufficient correlation between the functional activity of the claimed polymerase mutants and a particular, known structure to satisfy the written description requirement. Applicants respectfully maintain that the specification provides sufficient description and guidance for the claimed compositions. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Double Patenting

The rejection of claims 51-58, 67 and 96-102 under the judicially created doctrine of obviousness-type double patenting over claims 16-29 and 51-84 of U.S. Patent No. 6,395,524, is respectfully traversed. Applicants respectfully request that the obviousness-type double patenting rejection be held in abeyance until there is an indication of allowable subject matter.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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